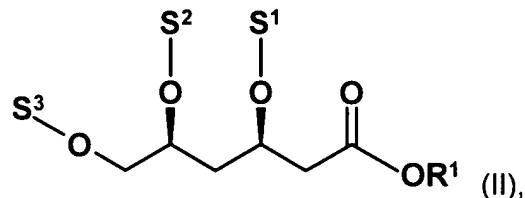


Patent claims:

5

1. Process for the preparation of a statin, comprising the following steps:

a) Preparation of a compound of the formula II



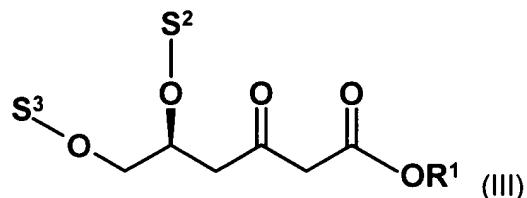
in which

S¹ denotes a hydrogen atom or a hydroxyl protective group,

S² and S³, independently of one another, denote hydroxyl protective groups and

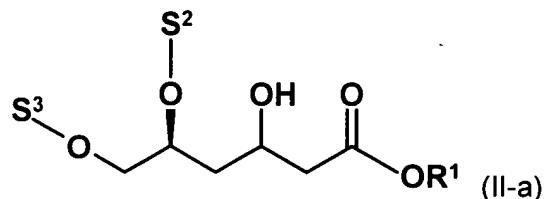
15 R¹ represents a hydrogen atom or a carboxyl protective group,

by stereoselective hydrogenation of a compound of the formula III



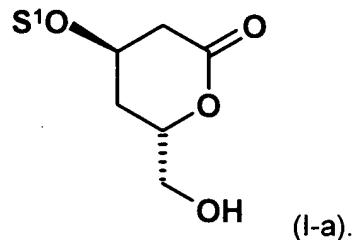
20

to give a compound of the formula II-a



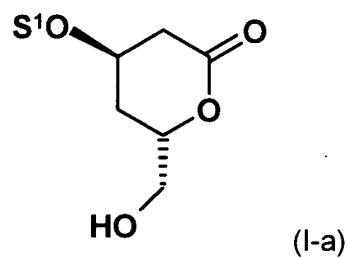
and optionally introduction of a hydroxyl protective group and

- b) lactonization of the compound of the formula II to give a compound of the formula I-a



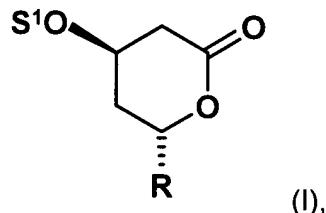
5 2. Process according to Claim 1, comprising the further step

- c) conversion of the compound of the formula I-a



10

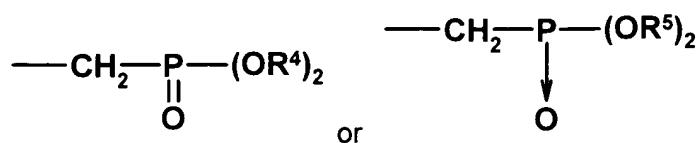
into a compound of the formula I



15 where the radical

S¹ is as defined in Claim 1,

R denotes -CH₂R², -CHO, -CH=P(R³)₃, -CH₂-P^{+(R³)₃M⁻,}



R² denotes a halogen atom, -C≡N, -CH₂NH₂, -SO₂-R⁶ or a leaving group,

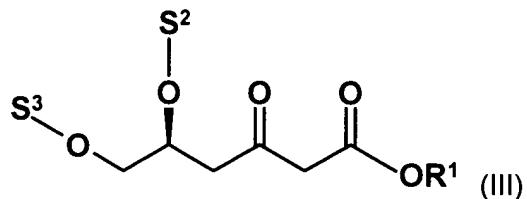
R³, R⁴ and R⁵ complete a Wittig radical or a Horner-Wittig radical,

R⁶ denotes a hydrogen atom or a C₁₋₃-alkyl or a C₅₋₁₀-aryl radical, which are optionally substituted by one or more radicals which, independently of one another, are selected from halogen atoms, heterocycles which contain 0 to 10 carbon atoms and 1 to 10 heteroatoms selected from sulphur, nitrogen and oxygen atoms, and functional groups and

M⁻ represents an opposite ion.

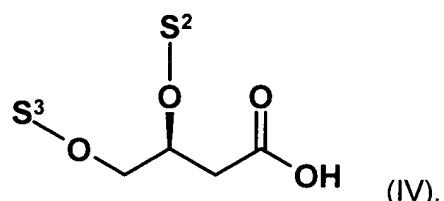
10 3. Process according to Claim 1 or 2, comprising the step:

preparation of a compound of the formula III



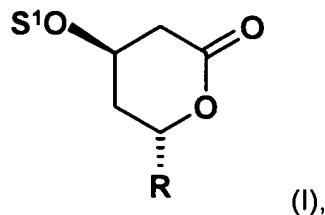
15

by chain extension of a compound of the formula IV



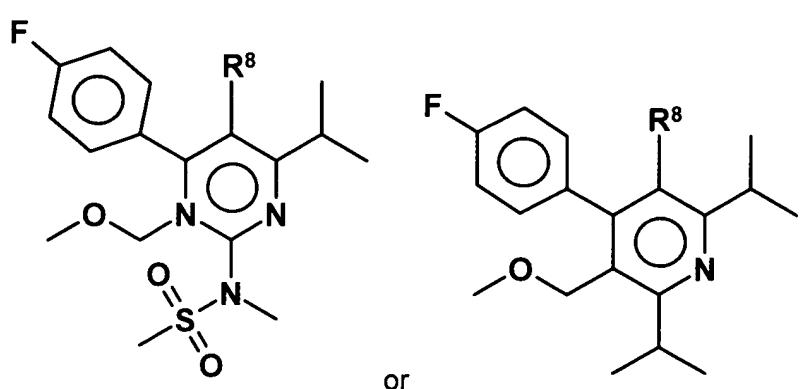
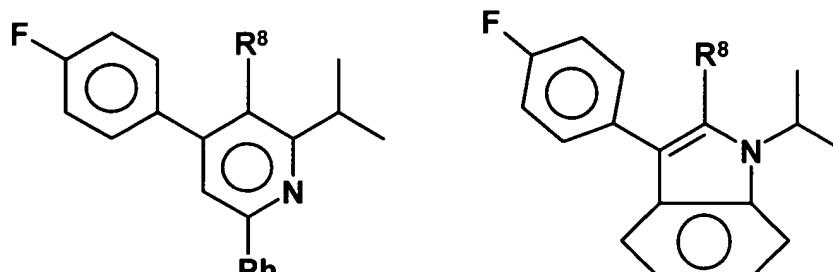
20 4. Process according to any of Claims 1 to 3, the compound of the formula I being converted into the statin by one of the following process steps and then optionally by opening of the lactone ring and optionally by removal of protective groups:

a) reaction of a compound of the formula (I)



in which the radical R represents a CHO group and the radical S^1 is as defined in Claim 1,

5 with a compound of the formula

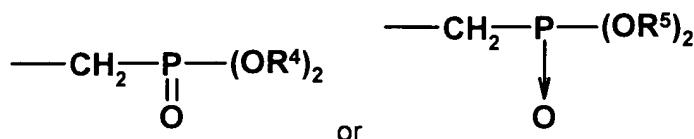


10

or

in which

R^8 denotes $-\text{CH}=\text{P}(\text{R}^3)_3$, $-\text{CH}_2\text{-P}^+(\text{R}^3)_3\text{M}^-$,

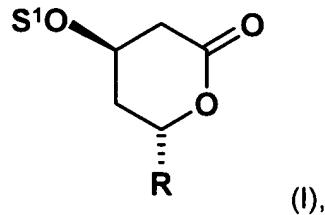


or

15 where R^3 , R^4 , R^5 and M are as defined in Claim 1,

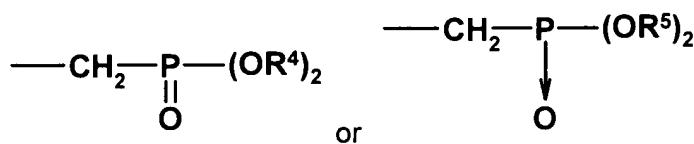
Atty Docket No.: LNK-014

b) reaction of a compound of the formula I



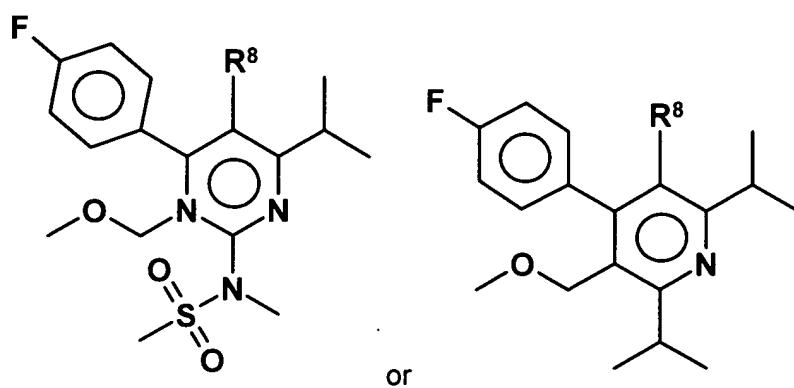
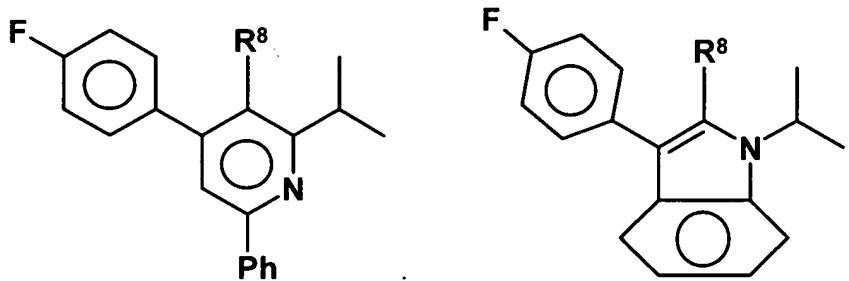
5 in which

the radical R denotes $-\text{CH}=\text{P}(\text{R}^3)_3$, $-\text{CH}_2\text{-P}^+(\text{R}^3)_3\text{M}^-$,



with a compound of the formula

10

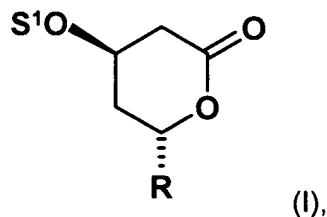


in which

15 R^8 denotes $-\text{CHO}$,

where R³, R⁴, R⁵ and M are as defined in Claim 1,

c) reaction of a compound of the formula I



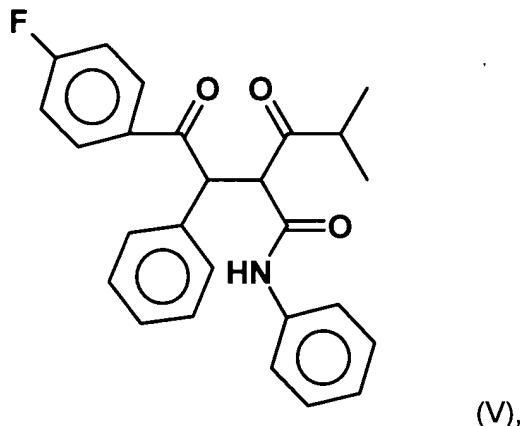
5 in which

the radical R is a group -CH₂-C≡N,

Hydrogenation of the compound of the formula I in which the radical R is a group -CH₂-C≡N, to give a compound of the formula I in which the radical R is a group -CH₂-CH₂NH₂.

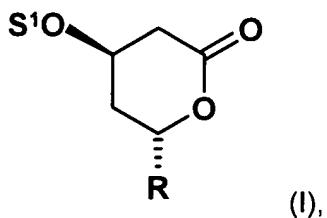
10

and reaction of the compound of the formula I in which the radical R is a group -CH₂-CH₂NH₂ with a compound of the formula V



15

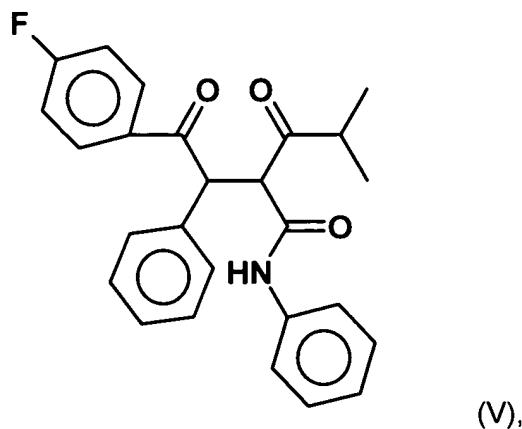
d) hydrogenation of a compound of the formula I



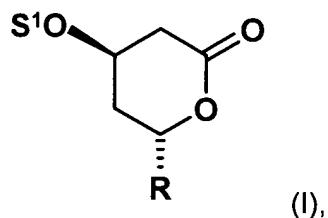
in which

the radical R is a group -CH₂-C≡N, to give a compound of the formula I in which the radical R is a group -CH₂-CH₂NH₂,

- 5 and reaction of the compound of the formula I in which the radical R is a group -CH₂-CH₂NH₂ with a compound of the formula V

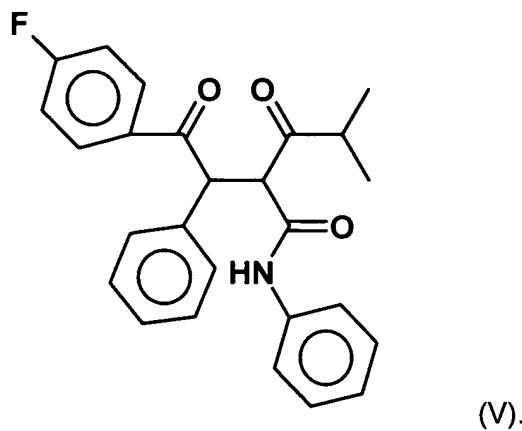


- 10 e) reaction of a compound of the formula (I)



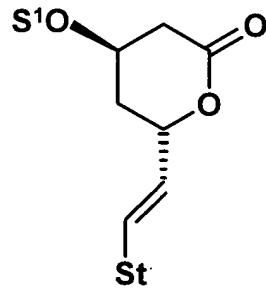
in which

- 15 the radical R is a group -CH₂-CH₂NH₂, with a compound of the formula V



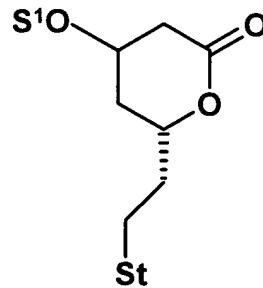
5. Process according any of Claims 1 to 4, characterized in that a compound of the formula

5



in which S¹ is as defined in Claim 1 and St represents the radical of the statin, is converted into a compound of the formula

10



by catalytic hydrogenation, and optionally the protective group S¹ is removed and optionally the lactone ring is opened.

15

6. Process according to any of Claims 1 to 5, the hydroxyl protective group S¹ being selected from a trimethylsilyl, triisopropylsilyl, trimethylsilyleethyl, tert-butyldimethylsilyl, tert-butylmethylsilyl, di-tert-butylmethysilyl, tert-butyldiphenylsilyl, triphenylsilyl, diphenylmethylsilyl, tris(trimethylsilyl) and para-tosyl protective group.

5

7. Process according to any of Claims 1 to 6, the protective groups S² and S³ being bridged.

8. Process according to Claim 7, the protective groups S² and S³ together representing an isopropylidene protective group.

10 9. Process according to any of Claims 2 to 7, the radical R representing a radical CH₂R² and R² representing a leaving group, the leaving group being selected from a halogen atom and a radical -OSO₂-C₁-C₆-alkyl or -OSO₂-C₅-C₁₀-aryl.

15

10. Process according to any of Claims 1 to 9, the radical R¹ denoting a hydrogen atom or a C₁₋₃-alkyl or C₄₋₁₀-aryl radical, which are optionally substituted by one or more radicals, which, independently of one another, are selected from halogen atoms, heterocycles which have 0 to 10 carbon atoms and 1 to 10 heteroatoms selected from sulphur, nitrogen and oxygen atoms, 20 and functional groups.

11. Process according to any of Claims 1 to 10,

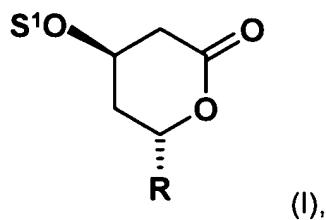
25 R³ denoting a C₅- to C₁₀-aryl radical which is optionally substituted by one or two C₁-C₄-alkyl radicals and/or halogen atoms, a C₁-C₄-alkyl radical or a C₅-C₁₀-cycloalkyl radical,

R⁴ denoting a C₁-C₄-alkyl radical,

R⁵ denoting a C₁-C₆-alkyl or C₅-C₁₀-aryl radical.

12. Process according to any of Claims 1 to 11, the statin being fluvastatin, rosuvastatin, 30 cerivastatin, glenvastatin or atorvastatin.

13. Compound of the formula I



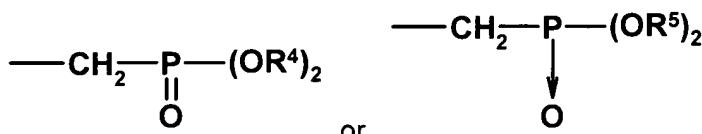
in which

S¹ and R are as defined in Claim 2, with the proviso that the radical S¹ does not represent a

5 tert-butyldimethylsilyl group if the radical R represents a CHO, -CH₂-OTos, -CH₂Cl or -CH₂I group.

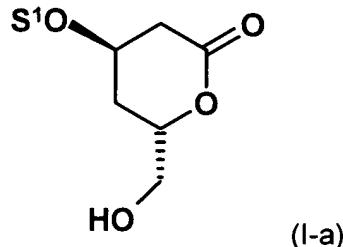
14. Compound according to Claim 13, in which the radical S¹ represents a tert-butyldimethylsilyl group and the radical R represents a -CH₂R², -CH=P(R³)₃, -CH₂-P⁺(R³)₃M⁻,

10



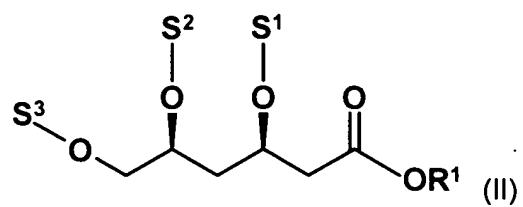
group, where R² represents a bromine atom, a -C≡N, a -CH₂NH₂ group or a radical -SO₂-R⁶, and R³, R⁴, R⁵, R⁶ and M are as defined in Claim 2.

15. 15. Process for the preparation of a compound of a formula (I-a)



in which the radical S¹ is as defined in Claim 1, characterized in that a compound of the formula II

20



in which

S^1 , S^2 , S^3 and R^1 are as defined in Claim 1, is converted into the compound of the formula I-a

- 5 by lactonization.